

DOCKET NO.: UPN-3827  
Application No.: 09/730,929  
Office Action Dated: November 14, 2002

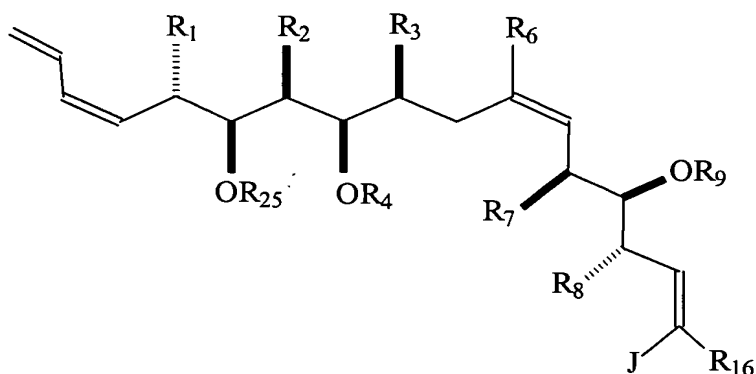
PATENT

Amendments to the Specification:

Please replace paragraph starting a page 23 line 12 with the following paragraph:

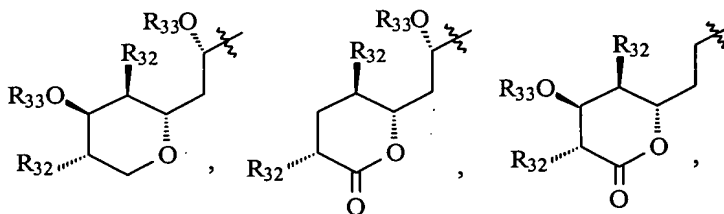
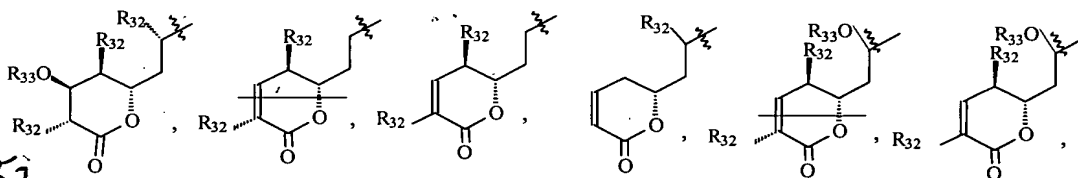
--The present invention also provides a process for forming a tetraene

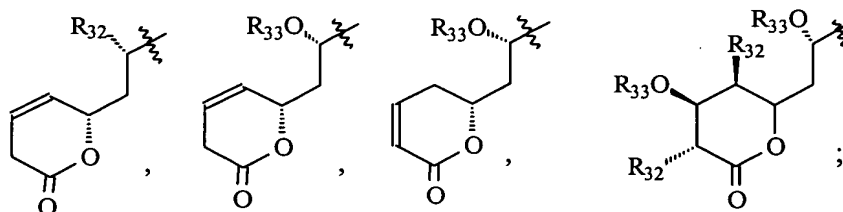
of formula:



wherein:

R<sub>1</sub>, R<sub>2</sub>, R<sub>7</sub>, and R<sub>8</sub> are independently C<sub>1</sub>-C<sub>10</sub> alkyl;  
R<sub>3</sub>, R<sub>6</sub>, and R<sub>16</sub> are independently selected from hydrogen and C<sub>1</sub>-C<sub>6</sub> alkyl;  
R<sub>4</sub> and R<sub>9</sub> are independently an acid labile hydroxyl protecting group;  
R<sub>25</sub> is an acid stable hydroxyl protecting group; and  
J is selected from:



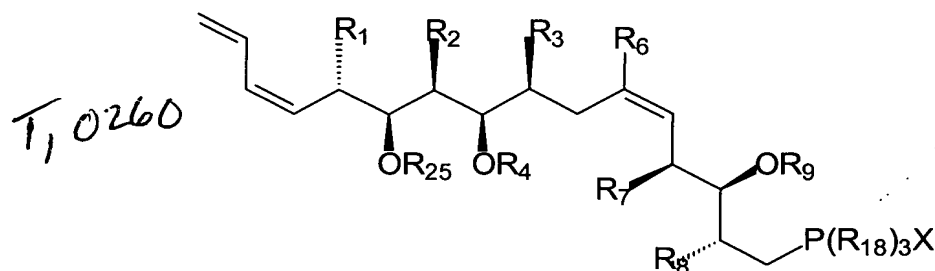


alkaryl; and alkheteroaryl;  
wherein

R<sub>32</sub> is H or C<sub>1</sub>-C<sub>6</sub> alkyl and R<sub>33</sub> is an acid labile hydroxyl protecting group;  
the process comprising contacting a compound of the formula:

J-CHO

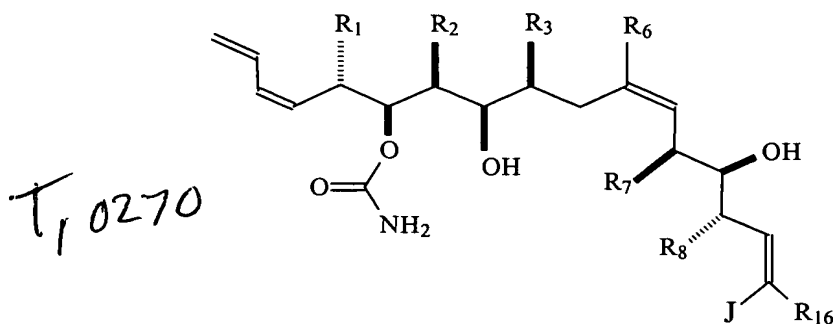
with a phosphonium salt of the formula:



wherein R<sub>18</sub> is C<sub>6</sub>-C<sub>14</sub> aryl, in the presence of a base for a time and under conditions effective to form the tetraene.--

Please replace paragraph starting a page 25 line 15 with the following paragraph:

--The present invention also provides a process for forming a tetraene  
of formula:



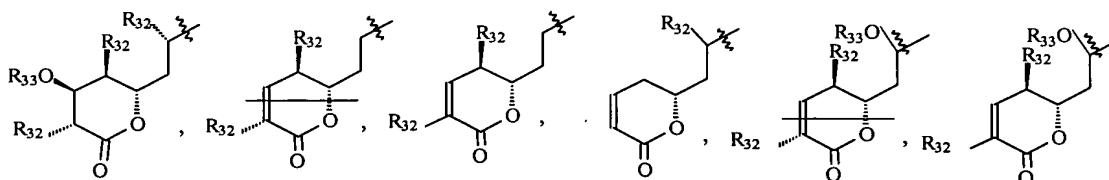
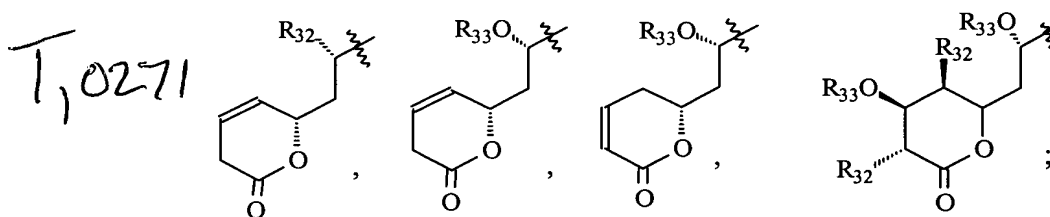
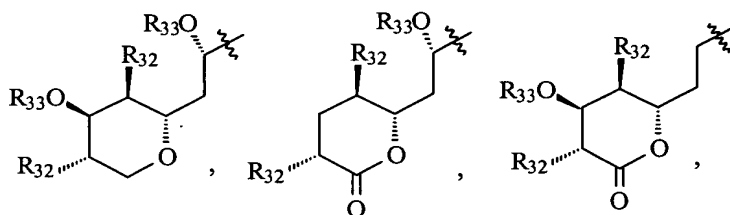
wherein:

R<sub>1</sub>, R<sub>2</sub>, R<sub>7</sub>, and R<sub>8</sub> are independently C<sub>1</sub>-C<sub>10</sub> alkyl;

R<sub>3</sub>, R<sub>6</sub>, and R<sub>16</sub> are independently selected from hydrogen and C<sub>1</sub>-C<sub>6</sub> alkyl; and

J is selected from:

J is selected from:



alkaryl, and alkheteroaryl;

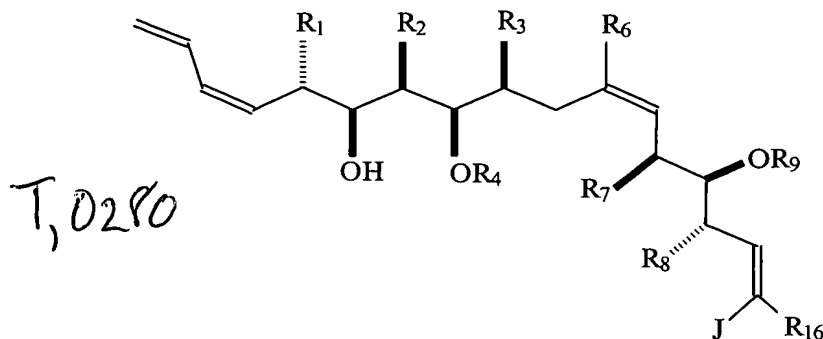
wherein

R<sub>32</sub> is H or C<sub>1</sub>-C<sub>6</sub> alkyl and R<sub>33</sub> is H;

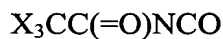
the process comprising contacting an alcohol of formula:

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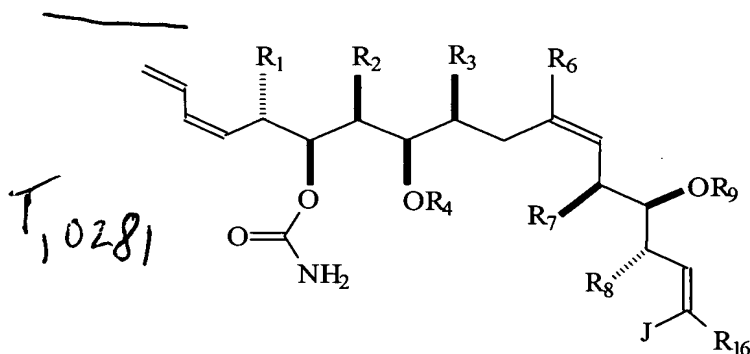


wherein R<sub>4</sub>, R<sub>9</sub>, and R<sub>33</sub> are acid labile hydroxyl protecting groups, with an isocyanate of the formula:



wherein X is a halogen, to form a carbamate intermediate;

contacting the carbamate intermediate with neutral alumina to form a carbamate of formula:



removing the acid labile hydroxyl protecting groups by contacting the carbamate with acid in a protic solvent to form the tetraene.--

Please replace paragraph starting a page 32 line 6 with the following paragraph:

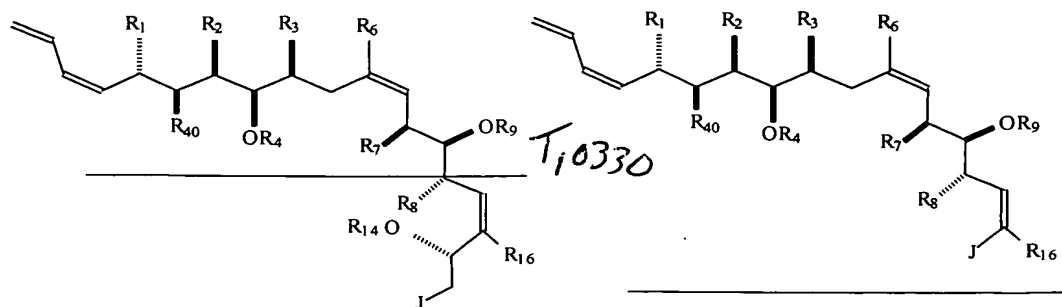
--The present invention also provides a compound of formula:

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wherein:

R<sub>1</sub>, R<sub>2</sub>, R<sub>7</sub>, and R<sub>8</sub> are independently C<sub>1</sub>-C<sub>10</sub> alkyl;

R<sub>3</sub>, R<sub>6</sub>, and R<sub>16</sub> are independently selected from hydrogen and C<sub>1</sub>-C<sub>6</sub>

alkyl;

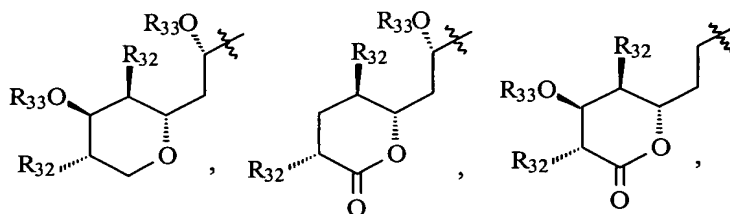
R<sub>4</sub>, R<sub>9</sub>, and R<sub>14</sub> are acid labile hydroxyl protecting groups;

R<sub>40</sub> is selected from OR<sub>25</sub> and OC(=O)NH<sub>2</sub>;

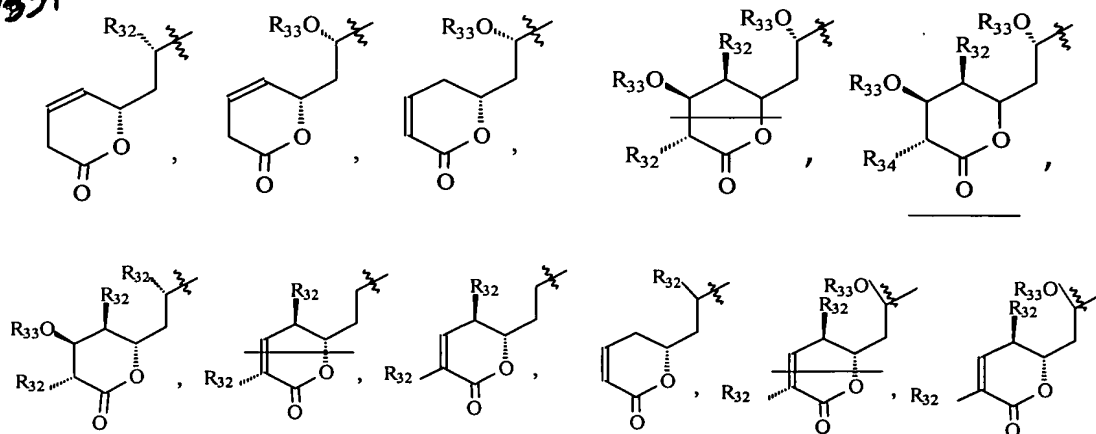
R<sub>25</sub> is an acid stable protecting group; and

J is selected from:

~~J is selected from:~~



T<sub>10331</sub>



alkaryl and alkheteroaryl;

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wherein

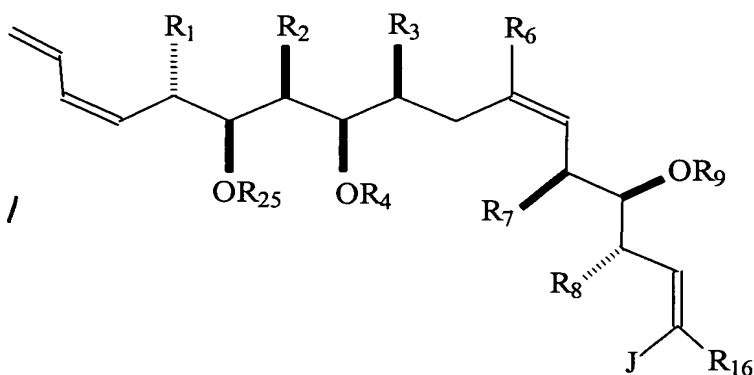
R<sub>32</sub> is C<sub>1</sub>-C<sub>6</sub> alkyl; and

R<sub>33</sub> is selected from H and an acid labile hydroxy protecting group; and

R<sub>34</sub> is C<sub>1</sub>-C<sub>6</sub> alkyl.

Please replace paragraph starting a page 62 line 10 with the following paragraph:

--The present invention further provides a process for forming a tetraene of formula:



wherein:

R<sub>1</sub>, R<sub>2</sub>, R<sub>7</sub>, and R<sub>8</sub> are independently C<sub>1</sub>-C<sub>10</sub> alkyl;

R<sub>3</sub>, R<sub>6</sub>, and R<sub>16</sub> are independently selected from hydrogen and C<sub>1</sub>-C<sub>6</sub>

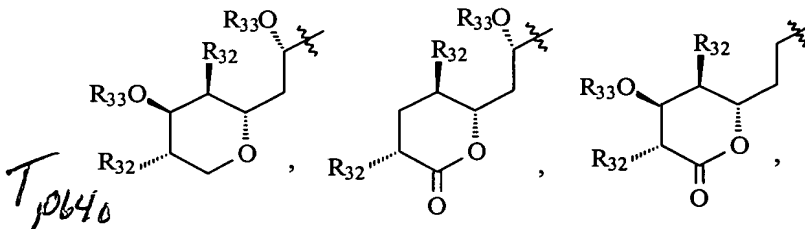
alkyl;

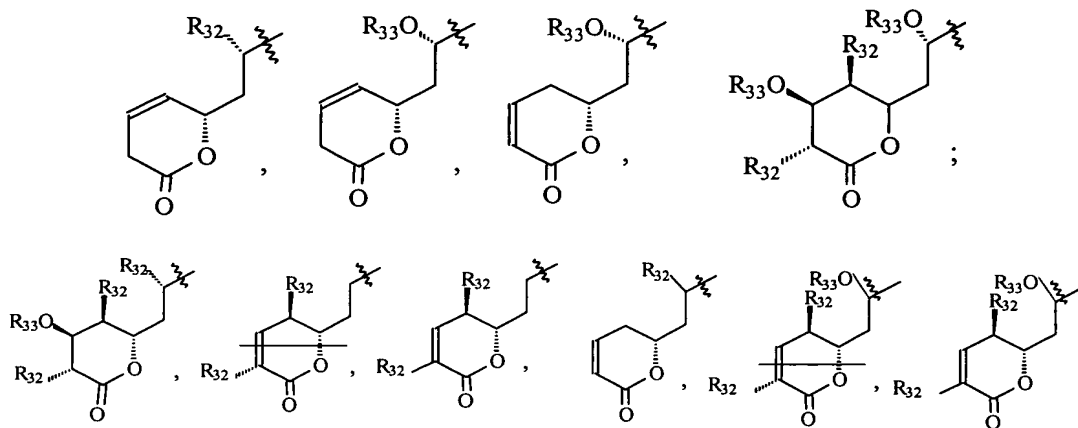
R<sub>4</sub> and R<sub>9</sub> are independently an acid labile hydroxyl protecting groups;

R<sub>25</sub> is an acid stable hydroxyl protecting group; and

J is selected from:

J is selected from:

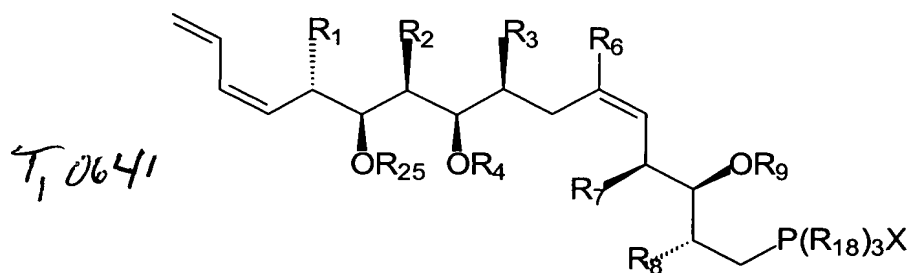




alkaryl, and alkheteroaryl;  
 wherein  $R_{32}$  is H or  $C_1$ - $C_6$  alkyl and  $R_{33}$  is H or an acid labile hydroxyl protecting group;  
 the process comprising contacting a compound of the formula:



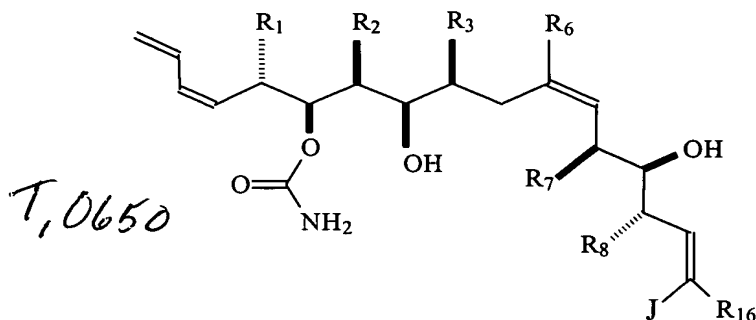
with a phosphonium salt of the formula:



wherein  $R_{18}$  is  $C_6$ - $C_{14}$  aryl, in the presence of a base for a time and under conditions effective to form the tetraene. In certain preferred embodiments, the process according to claim 11 wherein  $R_1$ ,  $R_2$ ,  $R_7$ , and  $R_8$  are independently  $C_1$ - $C_4$  alkyl,  $R_3$  and  $R_6$  are independently selected from hydrogen and  $C_1$ - $C_4$  alkyl, and  $R_{32}$  is  $C_{1-4}$  alkyl.--

Please replace paragraph starting a page 64 line 7 with the following paragraph:

--The present invention also provides a process for forming a tetraene of formula:



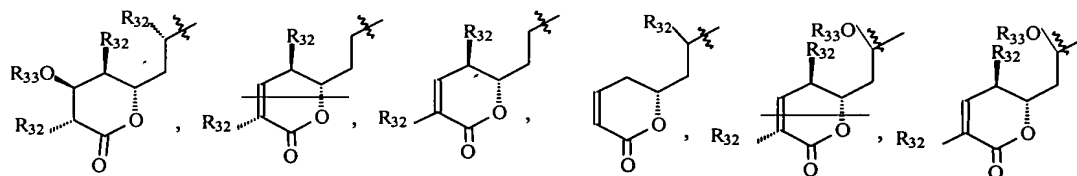
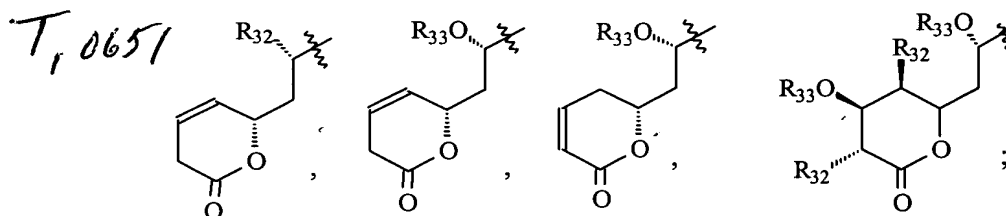
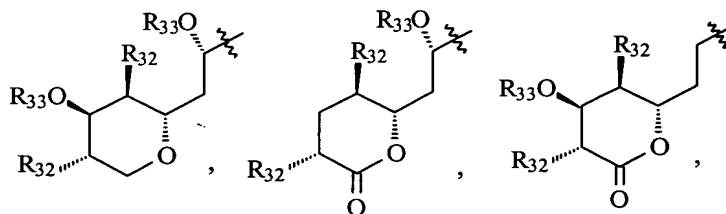
wherein:

R<sub>1</sub>, R<sub>2</sub>, R<sub>7</sub>, and R<sub>8</sub> are independently C<sub>1</sub>-C<sub>10</sub> alkyl;

R<sub>3</sub>, R<sub>6</sub>, and R<sub>16</sub> are independently selected from hydrogen and C<sub>1</sub>-C<sub>6</sub> alkyl; and

J is selected from:

J is selected from:

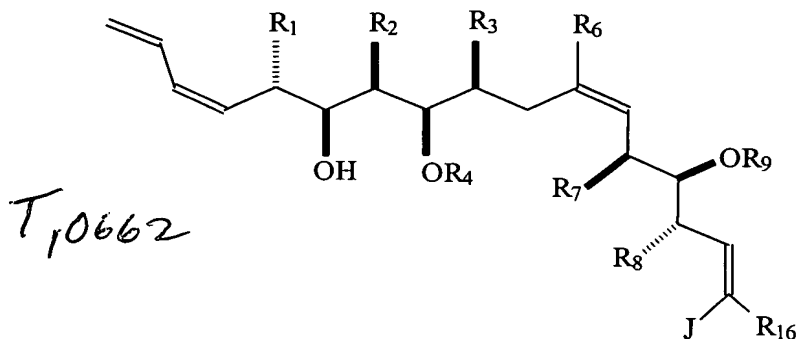


alkaryl, and alkheteroaryl;

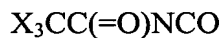
wherein R<sub>32</sub> is H or C<sub>1</sub>-C<sub>6</sub> alkyl and R<sub>33</sub> is H;

the process comprising contacting an alcohol of formula:

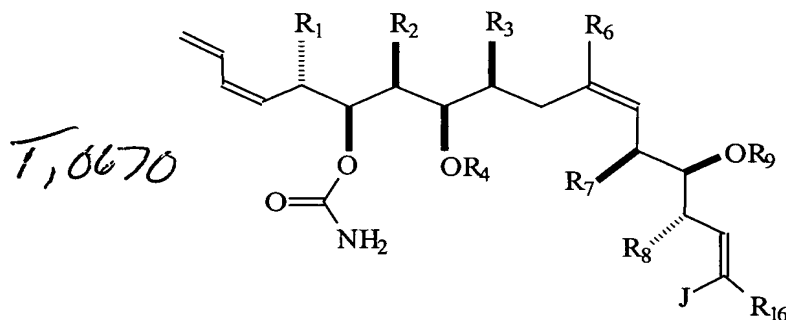




wherein R<sub>4</sub>, R<sub>9</sub>, and R<sub>33</sub> are acid labile hydroxyl protecting groups, with an isocyanate of the formula:



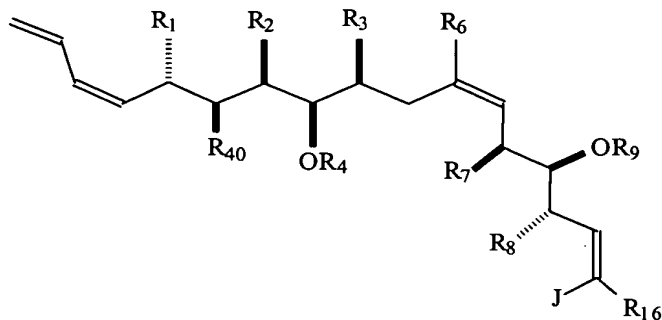
wherein X is a halogen, to form a carbamate intermediate;  
contacting the carbamate intermediate with neutral alumina to form a carbamate of formula:



and;  
removing the acid labile hydroxyl protecting groups by contacting the carbamate with acid in a protic solvent to form the tetraene.--

Please replace paragraph starting a page 70 line 19 with the following paragraph:

--In other embodiments, the present invention provides a compound of formula:

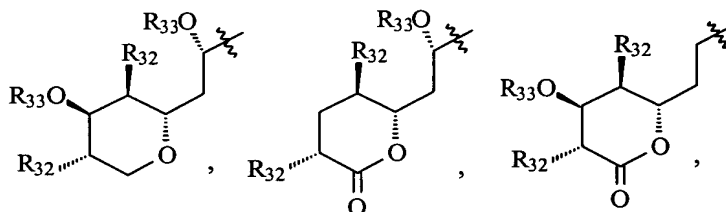


T, 0711

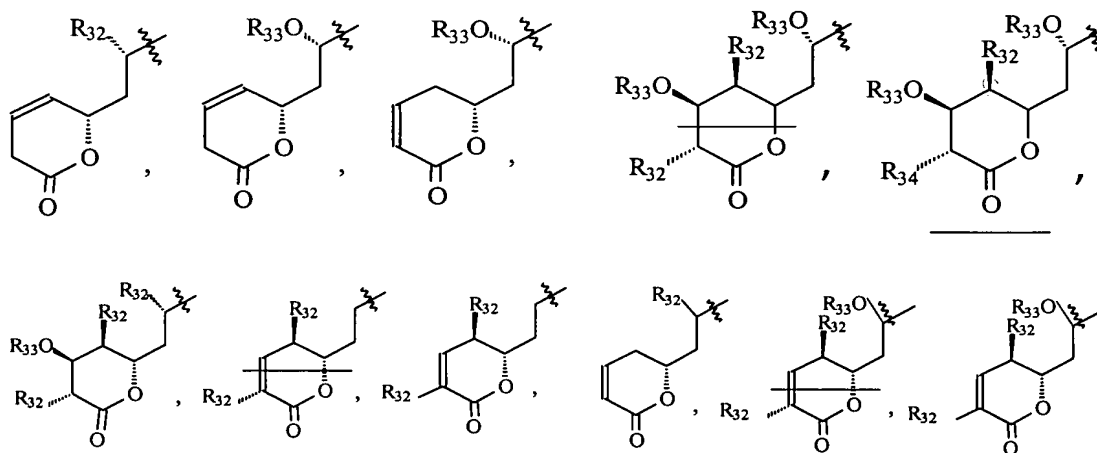
wherein:

R<sub>1</sub>, R<sub>2</sub>, R<sub>7</sub>, and R<sub>8</sub> are independently C<sub>1</sub>-C<sub>10</sub> alkyl;  
 R<sub>3</sub>, R<sub>6</sub>, and R<sub>16</sub> are independently selected from hydrogen and C<sub>1</sub>-C<sub>6</sub> alkyl;

R<sub>4</sub>, R<sub>9</sub>, and R<sub>14</sub> are acid labile hydroxyl protecting groups;  
 R<sub>40</sub> is selected from OR<sub>25</sub> and OC(=O)NH<sub>2</sub>;  
 R<sub>25</sub> is an acid stable protecting group; and  
 J is selected from:



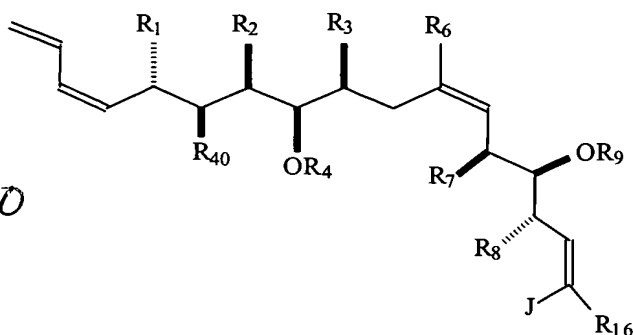
T, 0720



wherein R<sub>32</sub> is C<sub>1</sub>-C<sub>6</sub> alkyl, and R<sub>33</sub> is selected from H and an acid labile hydroxy protecting group, and R<sub>34</sub> is C<sub>1</sub>-C<sub>6</sub> alkyl.--

Please replace paragraph starting a page 71 line 14 with the following paragraph:

--The present invention also provides a compound of formula:



wherein:

R<sub>1</sub>, R<sub>2</sub>, R<sub>7</sub>, and R<sub>8</sub> are independently selected from hydrogen and C<sub>1</sub>-C<sub>10</sub> alkyl;

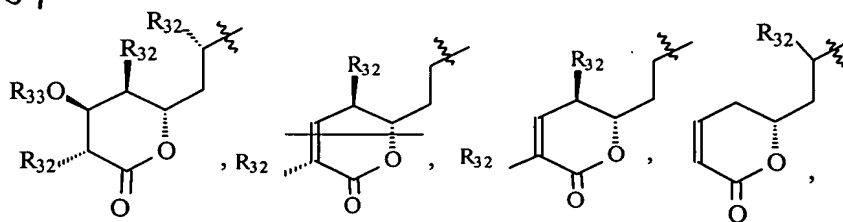
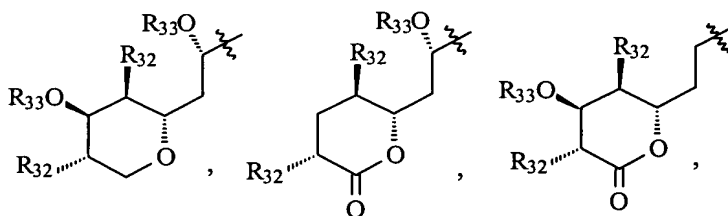
R<sub>3</sub>, R<sub>6</sub>, and R<sub>16</sub> are independently selected from hydrogen and C<sub>1</sub>-C<sub>6</sub> alkyl;

R<sub>4</sub> and R<sub>9</sub> are selected from hydrogen and acid labile hydroxyl protecting groups;

R<sub>40</sub> is selected from OR<sub>25</sub> and OC(=O)NH<sub>2</sub>;

R<sub>25</sub> is selected from hydrogen and an oxidatively labile protecting group; and

J is selected from:

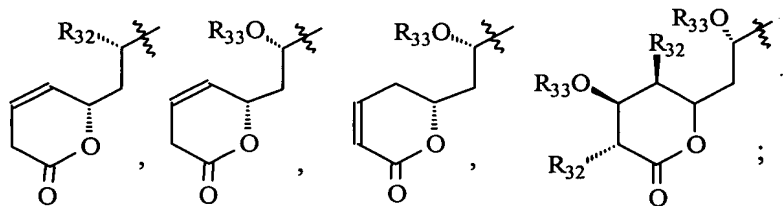


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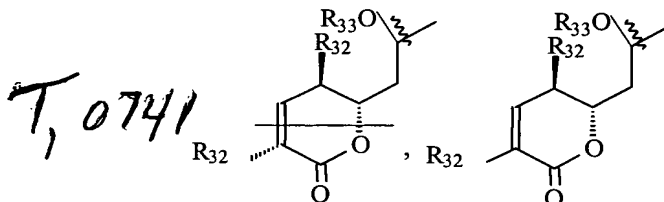
alkaryl and alkheteroaryl wherein aryl and heteroaryl are optionally substituted and alk is optionally substituted with  $R_{32}$  or  $OR_{33}$ ; wherein:

$R_{32}$  is selected from hydrogen and  $C_1$ - $C_6$  alkyl; and

$R_{33}$  is selected from hydrogen and an acid labile hydroxy protecting group. In certain embodiments,  $R^6$  is H.--

Please replace paragraph starting a page 73 line 15 with the following paragraph:

--In other preferred embodiments,  $R_1$ ,  $R_2$ ,  $R_6$ ,  $R_7$ , and  $R_8$  are methyl;  $R_4$  and  $R_9$  are H;  $R_{40}$  is  $-OC(O)NH_2$ ; and J is



wherein  $R_{32}$  is methyl and  $R_{33}$  is H.--

Please replace paragraph starting a page 74 line 4 with the following paragraph:

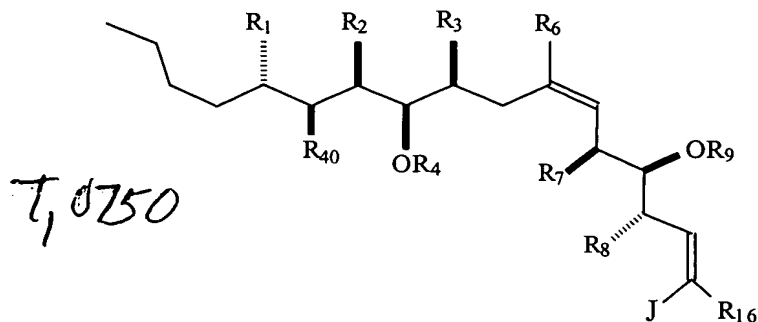
--In certain preferred embodiments, the present invention provides a compound having the following formula:

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wherein:

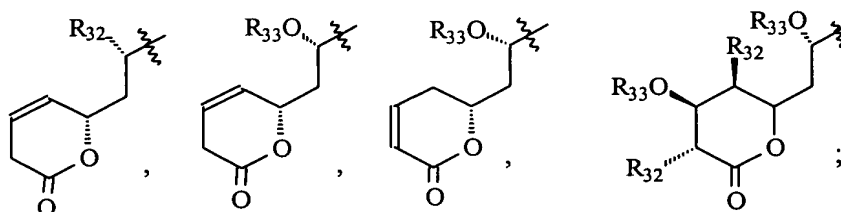
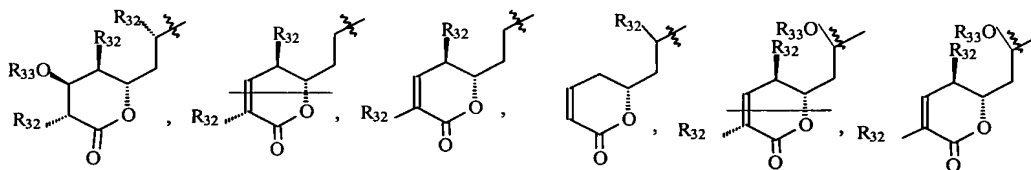
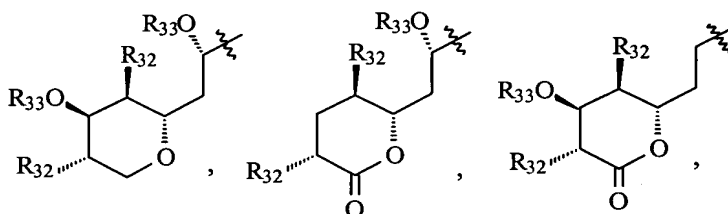
R<sub>1</sub>, R<sub>2</sub>, R<sub>7</sub>, and R<sub>8</sub> are independently hydrogen or C<sub>1</sub>-C<sub>10</sub> alkyl;

R<sub>3</sub>, R<sub>6</sub>, and R<sub>16</sub> are independently hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;

R<sub>4</sub> and R<sub>9</sub> are independently hydrogen or acid labile hydroxyl protecting groups;

R<sub>40</sub> is selected from OR<sub>25</sub> and OC(=O)NH<sub>2</sub>;

R<sub>25</sub> is hydrogen or an oxidatively labile protecting group; and J is selected from:



alkaryl and alkheteroaryl wherein aryl and heteroaryl are optionally substituted and alk is optionally substituted with R<sub>32</sub> or OR<sub>33</sub>;

wherein

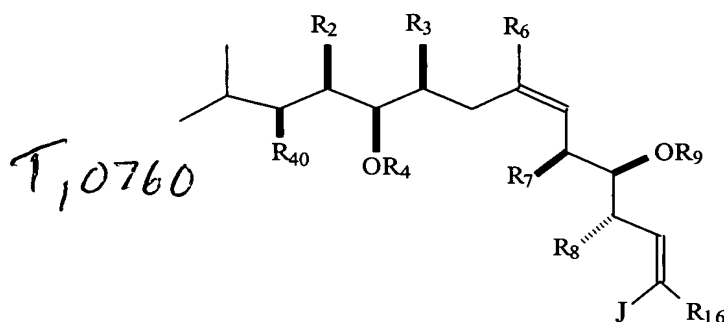
R<sub>32</sub> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl; and

A<sup>9</sup>  
Cont

R<sub>33</sub> is hydrogen or an acid labile hydroxy protecting group. In certain preferred embodiments, R<sub>6</sub> is H. In other embodiments, R<sub>1</sub>, R<sub>2</sub>, R<sub>7</sub>, and R<sub>8</sub> are methyl. In other embodiments, R<sub>4</sub>, R<sub>9</sub>, and R<sub>33</sub> are hydrogen. In other embodiments, R<sub>1</sub>, R<sub>2</sub>, R<sub>7</sub>, and R<sub>8</sub> are methyl; R<sub>4</sub>, R<sub>6</sub>, R<sub>9</sub>, and R<sub>33</sub> are H; and R<sub>40</sub> is -OC(O)NH<sub>2</sub>.

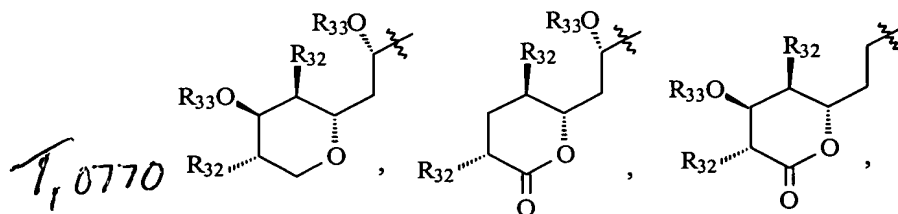
✓  
Please replace paragraph starting a page 75 line 13 with the following paragraph:

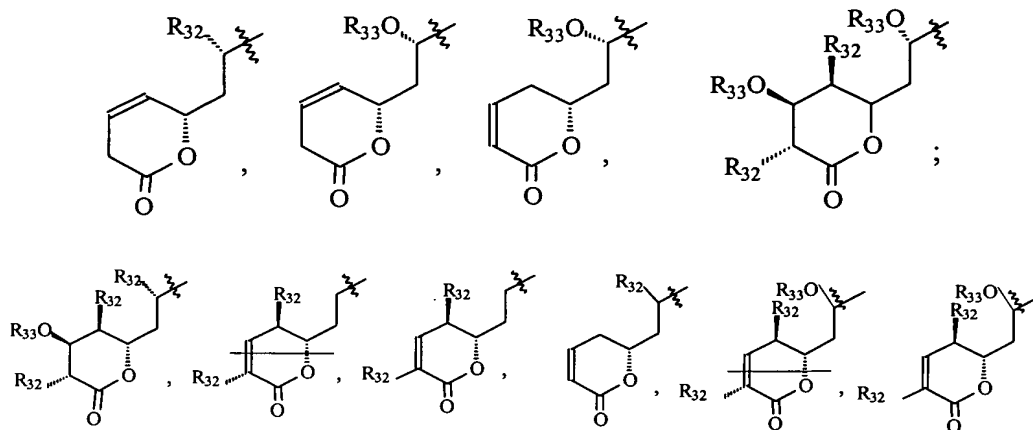
--In certain embodiments, the present invention provides a compounds  
having the formula:



wherein

- R<sub>2</sub>, R<sub>7</sub>, and R<sub>8</sub> are independently hydrogen or C<sub>1</sub>-C<sub>10</sub> alkyl;
- R<sub>3</sub>, R<sub>6</sub>, and R<sub>16</sub> are independently hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;
- R<sub>4</sub>, R<sub>9</sub>, and R<sub>33</sub> are independently hydrogen or acid labile hydroxyl protecting groups;
- ~~R<sub>4</sub> and R<sub>9</sub> are independently hydrogen or acid labile protecting hydroxyl groups;~~
- R<sub>40</sub> is selected from OR<sub>25</sub> and OC(=O)NH<sub>2</sub>;
- R<sub>25</sub> is hydrogen or an oxidatively labile protecting group; and
- J is selected from:





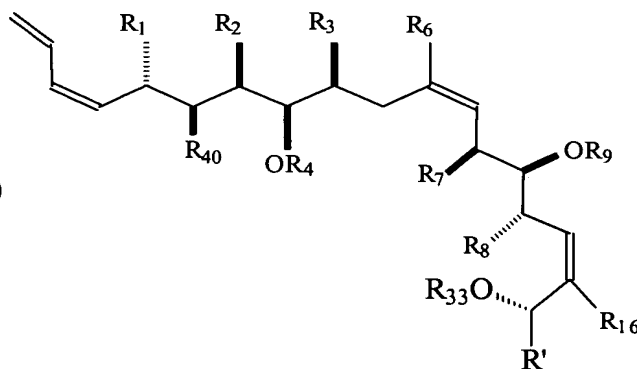
alkaryl and alkheteroaryl wherein aryl and heteroaryl are optionally substituted and alk is optionally substituted with R<sub>32</sub> or OR<sub>33</sub>;  
 wherein

R<sub>32</sub> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl; and

R<sub>33</sub> is hydrogen or an acid labile hydroxy protecting group.--

Please replace paragraph starting a page 76 line 17 with the following paragraph:

--In certain embodiments, the present invention provides a compound having the formula:



wherein:

R<sub>1</sub>, R<sub>2</sub>, R<sub>7</sub>, and R<sub>8</sub> are independently hydrogen or C<sub>1</sub>-C<sub>10</sub> alkyl;

R<sub>3</sub>, R<sub>6</sub>, and R<sub>16</sub> are independently hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;

R<sub>4</sub>, R<sub>9</sub>, and R<sub>33</sub> are independently hydrogen or acid labile hydroxy protecting groups;

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~~R<sub>4</sub>, R<sub>9</sub>, are independently hydrogen or acid labile protecting hydroxyl~~  
groups;

R<sub>25</sub> is hydrogen or an oxidatively labile protecting group;

R<sub>40</sub> is selected from OR<sub>25</sub> and OC(=O)NH<sub>2</sub>; ~~and~~

R' is methyl or alkyl-R"; and

R" is C<sub>1</sub>-C<sub>10</sub> alkoxy, hydroxy, or -C(O)CH<sub>3</sub>.--

All  
com.

a